## WE CLAIM

 A method for the treatment and/or prophylaxis of a Flaviviridae infection or disease associated with abnormal cellular proliferation in a host in need thereof, comprising administering to said host an effective treatment amount of a β-Dnucleoside of the general formula (IV-a\*):

$$W_{i/}^{2} - Z_{i}^{2}$$
 $W^{1}$ 
 $X^{2}$ 
 $X^{3}$ 
 $X^{2}$ 
 $X^{2}$ 
 $X^{2}$ 
 $X^{2}$ 
 $X^{2}$ 
 $X^{2}$ 
 $X^{3}$ 
 $X^{2}$ 
 $X^{2}$ 

or a pharmaceutically acceptable salt and/or prodrug thereof, wherein:

each D<sup>2</sup> is independently OH, SH, NH<sub>2</sub>, NHR<sup>4</sup>, or OD, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate, monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid;

each  $Z^1$  is independently O, S, CH<sub>2</sub>, CF<sub>2</sub>, C(=O), or C(=CH<sub>2</sub>); each  $Z^2$  is independently O, S, Se, C(=O), C(=S), C(=CH<sub>2</sub>), NH, or NR<sup>5</sup>;

each  $W^1$  and  $W^2$  is independently N or  $CR^{1'}$ ;

each R<sup>1</sup> is independently hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, Pr, i-Pr, n-Bu, i-Bu, t-Bu, CH<sub>2</sub>CN, CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>C(=O)NH<sub>2</sub>, CH<sub>2</sub>C(=S)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, C(=S)NH<sub>2</sub>, C(=NH)NH<sub>2</sub>, C(=O)NHOH, C(=O)NHNH<sub>2</sub>, CH<sub>2</sub>NH<sub>3</sub>, NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, NHCH<sub>2</sub>CH<sub>3</sub>, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, SH, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>H, CN, or CHR\*NH<sub>2</sub>;

each R\* is hydrogen, F, Cl, Br, or I;

each R<sup>2'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

5

15

20

each R<sup>3'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>4</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, lower haloalkyl, optionally substituted or unsubstituted lower alkenyl, lower haloalkenyl, optionally substituted or unsubstituted aryl, arylalkyl such as unsubstituted or substituted phenyl or benzyl, or an optionally substituted or unsubstituted acyl;

each R<sup>5</sup> is independently hydrogen, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, Pr, i-Pr, n-Bu, i-Bu, t-Bu, CH<sub>2</sub>CN, CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>C(=O)NH<sub>2</sub>, CH<sub>2</sub>C(=S)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, or C(=S)NH<sub>2</sub>; and

such that there are no more than three ring-heteroatoms;

optionally in a pharmaceutically acceptable carrier or diluent.

- 2. The method of claim 1, wherein  $Z^1$  is O.
- 3. The method of claim 1, wherein  $Z^1$  is S.
- 15 4. The method of claim 1, wherein  $Z^1$  is  $CH_2$ .

5

10

20

- 5. The method of claim 1, wherein  $Z^1$  is  $CF_2$ .
- 6. A method for the treatment and/or prophylaxis of a Flaviviridae infection or disease associated with abnormal cellular proliferation in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the general formula (IV-b\*):

$$W_{j}^{2}=W^{3}$$

$$W^{1}$$

$$Y^{1}$$

$$R^{3'}$$

$$R^{2'}$$
[IV-b\*]

or a pharmaceutically acceptable salt and/or prodrug thereof, wherein:

each D<sup>2</sup> is independently OH, SH, NH<sub>2</sub>, NHR<sup>4</sup>, or OD, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate,

monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid;

each Z<sup>1</sup> is independently O, S, CH<sub>2</sub>, CF<sub>2</sub>, C(=O), or C(=CH<sub>2</sub>);

each Y<sup>1</sup> is independently O, S, Se, or NH;

5

10

15

20

each W1 and W2 is independently N or CR1';

each W<sup>3</sup> is independently N, CH, CCH<sub>3</sub>, CF, CCl, CBr, CI, CCO<sub>2</sub>H, CCO<sub>2</sub>CH<sub>3</sub>, CCONH<sub>2</sub>, CC(=S)NH<sub>2</sub>, or CCN;

each R<sup>1</sup> is independently hydrogen, halogen (F, Cl, Br or I), CH<sub>3</sub> (Me), CH<sub>2</sub>CH<sub>3</sub> (Et), Pr, i-Pr, n-Bu, i-Bu, t-Bu, CH<sub>2</sub>CN, CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>C(=O)NH<sub>2</sub>, CH<sub>2</sub>C(=S)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, C(=S)NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, NHCH<sub>2</sub>CH<sub>3</sub>, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, SH, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>H, or CN;

each R<sup>2'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>3'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>; and

each R<sup>4</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, lower haloalkyl, optionally substituted or unsubstituted lower alkenyl, lower haloalkenyl, optionally substituted or unsubstituted aryl, arylalkyl such as unsubstituted or substituted phenyl or benzyl, or an optionally substituted or unsubstituted acyl;

optionally in a pharmaceutically acceptable carrier or diluent.

- 7. The method of claim 6, wherein  $Z^1$  is O.
- 8. The method of claim 6, wherein  $Z^1$  is S.
- 25 9. The method of claim 6, wherein  $Z^1$  is  $CH_2$ .
  - 10. The method of claim 6, wherein  $Z^1$  is  $CF_2$ .

11. A method for the treatment and/or prophylaxis of a Flaviviridae infection or disease associated with abnormal cellular proliferation in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the general formula (IV-c\*):

$$D^{2}$$

$$R^{3'}$$

$$R^{2'}$$

$$R^{2'}$$

$$R^{2'}$$

$$R^{2'}$$

or a pharmaceutically acceptable salt and/or prodrug thereof, wherein:

5

10

15

20

each D<sup>2</sup> is independently OH, SH, NH<sub>2</sub>, NHR<sup>4</sup>, or OD, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate, monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid;

each Z<sup>1</sup> is independently O, S, CH<sub>2</sub>, CF<sub>2</sub>, C(=O), or C(=CH<sub>2</sub>);

each Y<sup>1</sup> is independently O, S, Se, or NH;

each  $W^1$ ,  $W^2$ , and  $W^3$  is independently N or  $CR^{1'}$ ;

each R<sup>1</sup> is independently hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, Pr, i-Pr, n-Bu, i-Bu, t-Bu, CH<sub>2</sub>CN, CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>C(=O)NH<sub>2</sub>, CH<sub>2</sub>C(=S)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, C(=S)NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, NHCH<sub>2</sub>CH<sub>3</sub>, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, SH, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>H, or CN;

each R<sup>2'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>3'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>; and

each R<sup>4</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, lower haloalkyl, optionally substituted or unsubstituted lower alkenyl, lower haloalkenyl, optionally substituted or unsubstituted aryl,

arylalkyl such as unsubstituted or substituted phenyl or benzyl, or an optionally substituted or unsubstituted acyl;

optionally in a pharmaceutically acceptable carrier or diluent.

- 12. The method of claim 11, wherein  $Z^1$  is O.
- 5 13. The method of claim 11, wherein  $Z^1$  is S.

10

15

20

- 14. The method of claim 11, wherein  $Z^1$  is  $CH_2$ .
- 15. The method of claim 11, wherein  $Z^1$  is  $CF_2$ .
- 16. A method for the treatment and/or prophylaxis of a *Flaviviridae* infection or disease associated with abnormal cellular proliferation in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the general formula (IV-d\*):

$$D^{2}$$

$$R^{1}$$

$$N$$

$$N$$

$$N$$

$$N$$

$$R^{2}$$

$$R^{3}$$

$$R^{2}$$

$$R^{2}$$

or a pharmaceutically acceptable salt and/or prodrug thereof, wherein:

each D<sup>2</sup> is independently OH, SH, NH<sub>2</sub>, NHR<sup>4</sup>, or OD, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate, monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid;

each Z<sup>1</sup> is independently O, S, CH<sub>2</sub>, CF<sub>2</sub>, C(=O), or C(=CH<sub>2</sub>);

each  $R^{1}$  is independently CN,  $CO_2CH_3$ ,  $C(=O)NH_2$ ,  $C(=S)NH_2$ , or  $C(=NH)NH_2$ ;

each R<sup>1"</sup> is independently OH, SH, NH<sub>2</sub>, or NHR<sup>5</sup>;

each R<sup>2'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>3'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>4</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, lower haloalkyl, optionally substituted or unsubstituted lower alkenyl, lower haloalkenyl, optionally substituted or unsubstituted aryl, arylalkyl such as unsubstituted or substituted phenyl or benzyl, or an optionally substituted or unsubstituted acyl; and

each R<sup>5</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, or an optionally substituted or unsubstituted acyl;

optionally in a pharmaceutically acceptable carrier or diluent.

17. The method of claim 16, wherein  $Z^1$  is O.

5

10

- 18. The method of claim 16, wherein  $Z^1$  is S.
- 19. The method of claim 16, wherein  $Z^1$  is  $CH_2$ .
- 20. The method of claim 16, wherein  $Z^1$  is  $CF_2$ .
- 21. A method for the treatment and/or prophylaxis of a *Flaviviridae* infection or disease associated with abnormal cellular proliferation in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the formula:

or a pharmaceutically acceptable salt and/or prodrug thereof, optionally in a pharmaceutically acceptable carrier or diluent.

22. A method for the treatment and/or prophylaxis of a *Flaviviridae* infection or disease associated with abnormal cellular proliferation in a host in need thereof,

comprising administering to said host an effective treatment amount of a  $\beta$ -D-nucleoside of the formula:

or a pharmaceutically acceptable salt and/or prodrug thereof, optionally in a pharmaceutically acceptable carrier or diluent.

23. A method for the treatment and/or prophylaxis of a *Flaviviridae* infection or disease associated with abnormal cellular proliferation in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the formula:

5

10

24. A method for the treatment and/or prophylaxis of a *Flaviviridae* infection or disease associated with abnormal cellular proliferation in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the formula:

or a pharmacoutically accomtable self and/an

5

10

- 25. A method for the treatment and/or prophylaxis of a *Flaviviridae* infection or disease associated with abnormal cellular proliferation in a host in need thereof, comprising administering to said host an effective treatment amount of N-(phosphonoacetyl)-L-aspartate (PALA), or its pharmaceutically acceptable salt and/or prodrug, optionally in a pharmaceutically acceptable carrier or diluent.
- 26. The method of claim 1, wherein the pharmaceutically acceptable carrier is suitable for oral delivery.
- 15 27. The method of claim 1, wherein the pharmaceutically acceptable carrier is suitable for intravenous delivery.
  - 28. The method of claim 1, wherein the pharmaceutically acceptable carrier is suitable for parenteral delivery.
- 29. The method of claim 1, wherein the pharmaceutically acceptable carrier is suitable for intradermal delivery.
  - 30. The method of claim 1, wherein the pharmaceutically acceptable carrier is suitable for subcutaneous delivery.
  - 31. The method of claim 1, wherein the pharmaceutically acceptable carrier is suitable for topical delivery.

- 32. The method of claim 1, wherein the effective compound is in the form of a dosage unit, such that said dosage unit contains 10 to 1500 mg of the compound.
- 33. The method of claim 1, wherein the effective compound is in the form of a dosage unit that is a tablet or capsule.
- 5 34. The method of claim 1, wherein the host is a human.

10

15

20

- 35. The method of claim 1, wherein the Flaviviridae infection is an HCV infection.
- 36. The method of claim 35, wherein the host is a human.
- 37. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the general formula (IV-a\*):

$$W_{l/}^{2} - Z_{l}^{2}$$
 $W^{1}$ 
 $N$ 
 $D^{2}$ 
 $R^{3'}$ 
 $R^{2'}$ 
[IV-a\*]

or a pharmaceutically acceptable salt and/or prodrug thereof, wherein:

each D<sup>2</sup> is independently OH, SH, NH<sub>2</sub>, NHR<sup>4</sup>, or OD, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate, monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid;

each  $Z^1$  is independently O, S, CH<sub>2</sub>, CF<sub>2</sub>, C(=O), or C(=CH<sub>2</sub>);

each Z<sup>2</sup> is independently O, S, Se, C(=O), C(=S), C(=CH<sub>2</sub>), NH, or NR<sup>5</sup>;

each  $W^1$  and  $W^2$  is independently N or  $CR^{1'}$ ;

each R<sup>1'</sup> is independently hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, Pr, i-Pr, n-Bu, i-Bu, t-Bu, CH<sub>2</sub>CN, CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>C(=O)NH<sub>2</sub>, CH<sub>2</sub>C(=S)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, C(=O)NH<sub>3</sub>, NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, NHCH<sub>2</sub>CH<sub>3</sub>, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, SH, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>H, CN, or CHR\*NH<sub>2</sub>;

each R\* is hydrogen, F, Cl, Br, or I;

5

10

15

each R<sup>2'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>3'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>4</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, lower haloalkyl, optionally substituted or unsubstituted lower alkenyl, lower haloalkenyl, optionally substituted or unsubstituted aryl, arylalkyl such as unsubstituted or substituted phenyl or benzyl, or an optionally substituted or unsubstituted acyl;

each  $R^5$  is independently hydrogen,  $CH_3$ ,  $CH_2CH_3$ , Pr, i-Pr, n-Bu, i-Bu, t-Bu,  $CH_2CN$ ,  $CH_2CO_2CH_3$ ,  $CH_2C(=O)NH_2$ ,  $CH_2C(=S)NH_2$ ,  $C(=O)NH_2$ , or  $C(=S)NH_2$ ; and

such that there are no more than three ring-heteroatoms;

optionally in a pharmaceutically acceptable carrier or diluent.

- 38. The method of claim 37, wherein  $Z^1$  is O.
- 39. The method of claim 37, wherein  $Z^1$  is S.
- 40. The method of claim 37, wherein  $Z^1$  is  $CH_2$ .
- 41. The method of claim 37, wherein  $Z^1$  is  $CF_2$ .
- 42. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the general formula (IV-b\*):

$$W_{j}^{2}=W^{3}$$

$$W^{1}$$

$$R^{3'}$$

$$R^{2'}$$
[IV-b\*]

or a pharmaceutically acceptable salt and/or prodrug thereof, wherein:

each D<sup>2</sup> is independently OH, SH, NH<sub>2</sub>, NHR<sup>4</sup>, or OD, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate, monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid;

each Z<sup>1</sup> is independently O, S, CH<sub>2</sub>, CF<sub>2</sub>, C(=O), or C(=CH<sub>2</sub>);

each Y<sup>1</sup> is independently O, S, Se, or NH;

5

10

15

20

25

each W1 and W2 is independently N or CR1;

each W<sup>3</sup> is independently N, CH, CCH<sub>3</sub>, CF, CCl, CBr, CI, CCO<sub>2</sub>H, CCO<sub>2</sub>CH<sub>3</sub>, CCONH<sub>2</sub>, CC(=S)NH<sub>2</sub>, or CCN;

each R<sup>1</sup> is independently hydrogen, halogen (F, Cl, Br or I), CH<sub>3</sub> (Me), CH<sub>2</sub>CH<sub>3</sub> (Et), Pr, i-Pr, n-Bu, i-Bu, t-Bu, CH<sub>2</sub>CN, CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>C(=O)NH<sub>2</sub>, CH<sub>2</sub>C(=S)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, C(=S)NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, NHCH<sub>2</sub>CH<sub>3</sub>, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, SH, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>H, or CN;

each R<sup>2'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>3'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>; and

each R<sup>4</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, lower haloalkyl, optionally substituted or unsubstituted lower alkenyl, lower haloalkenyl, optionally substituted or unsubstituted aryl, arylalkyl such as unsubstituted or substituted phenyl or benzyl, or an optionally substituted or unsubstituted acyl;

optionally in a pharmaceutically acceptable carrier or diluent.

- 43. The method of claim 42, wherein  $Z^1$  is O.
- 44. The method of claim 42, wherein  $Z^1$  is S.
- 45. The method of claim 42, wherein  $Z^1$  is  $CH_2$ .

79

- 46. The method of claim 42, wherein  $Z^1$  is  $CF_2$ .
- 47. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the general formula (IV-c\*):

$$D^{2} \xrightarrow{\mathbb{R}^{3'}} \mathbb{R}^{2'}$$

$$[IV-c*]$$

5

or a pharmaceutically acceptable salt and/or prodrug thereof, wherein:

each D<sup>2</sup> is independently OH, SH, NH<sub>2</sub>, NHR<sup>4</sup>, or OD, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate, monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid;

10

each Z<sup>1</sup> is independently O, S, CH<sub>2</sub>, CF<sub>2</sub>, C(=O), or C(=CH<sub>2</sub>);

each Y<sup>1</sup> is independently O, S, Se, or NH;

each W1, W2, and W3 is independently N or CR1';

15

each R<sup>1</sup> is independently hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, Pr, i-Pr, n-Bu, i-Bu, t-Bu, CH<sub>2</sub>CN, CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>C(=O)NH<sub>2</sub>, CH<sub>2</sub>C(=S)NH<sub>2</sub>, C(=O)NH<sub>2</sub>, C(=S)NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, NHCH<sub>2</sub>CH<sub>3</sub>, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, SH, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>H, or CN;

each R<sup>2'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

20

each R<sup>3'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>; and

each R<sup>4</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, lower haloalkyl, optionally substituted or unsubstituted lower alkenyl, lower haloalkenyl, optionally substituted or unsubstituted aryl,

arylalkyl such as unsubstituted or substituted phenyl or benzyl, or an optionally substituted or unsubstituted acyl;

optionally in a pharmaceutically acceptable carrier or diluent.

- 48. The method of claim 47, wherein  $Z^1$  is O.
- 5 49. The method of claim 47, wherein  $Z^1$  is S.

10

15

20

- 50. The method of claim 47, wherein  $Z^1$  is  $CH_2$ .
- 51. The method of claim 47, wherein  $Z^1$  is  $CF_2$ .
- 52. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the general formula (IV-d\*):

$$D^{2}$$

$$R^{1}$$

or a pharmaceutically acceptable salt and/or prodrug thereof, wherein:

each  $D^2$  is independently OH, SH, NH<sub>2</sub>, NHR<sup>4</sup>, or OD, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate, monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid;

each Z<sup>1</sup> is independently O, S, CH<sub>2</sub>, CF<sub>2</sub>, C(=O), or C(=CH<sub>2</sub>);

each  $R^{1'}$  is independently CN,  $CO_2CH_3$ ,  $C(=O)NH_2$ ,  $C(=S)NH_2$ , or  $C(=NH)NH_2$ ;

each R<sup>1"</sup> is independently OH, SH, NH<sub>2</sub>, or NHR<sup>5</sup>;

each R<sup>2'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>3'</sup> independently is hydrogen, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>F, CH<sub>2</sub>SH, CH<sub>2</sub>SCH<sub>3</sub>, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, OH, OCH<sub>3</sub>, or NH<sub>2</sub>;

each R<sup>4</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, lower haloalkyl, optionally substituted or unsubstituted lower alkenyl, lower haloalkenyl, optionally substituted or unsubstituted aryl, arylalkyl such as unsubstituted or substituted phenyl or benzyl, or an optionally substituted or unsubstituted acyl; and

each R<sup>5</sup> is independently is hydrogen, optionally substituted or unsubstituted lower alkyl, or an optionally substituted or unsubstituted acyl;

optionally in a pharmaceutically acceptable carrier or diluent.

53. The method of claim 52, wherein  $Z^1$  is O.

5

10

- 54. The method of claim 52, wherein  $Z^1$  is S.
- 55. The method of claim 52, wherein  $Z^1$  is  $CH_2$ .
- 56. The method of claim 52, wherein  $Z^1$  is  $CF_2$ .
- 57. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the formula:

58. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the formula:

- or a pharmaceutically acceptable salt and/or prodrug thereof, optionally in a pharmaceutically acceptable carrier or diluent.
  - 59. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the formula:

10

60. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of a β-D-nucleoside of the formula:

or a pharmaceutically acceptable salt and/or prodrug thereof, optionally in a pharmaceutically acceptable carrier or diluent.

10

- 61. A method for the treatment and/or prophylaxis of an HCV infection in a host in need thereof, comprising administering to said host an effective treatment amount of N-(phosphonoacetyl)-L-aspartate (PALA), or its pharmaceutically acceptable salt and/or prodrug, optionally in a pharmaceutically acceptable carrier or diluent.
- 62. The method of claim 37, wherein the pharmaceutically acceptable carrier is suitable for oral delivery.
- 63. The method of claim 37, wherein the pharmaceutically acceptable carrier is suitable for intravenous delivery.
- 15 64. The method of claim 37, wherein the pharmaceutically acceptable carrier is suitable for parenteral delivery.
  - 65. The method of claim 37, wherein the pharmaceutically acceptable carrier is suitable for intradermal delivery.
- 66. The method of claim 37, wherein the pharmaceutically acceptable carrier is suitable for subcutaneous delivery.
  - 67. The method of claim 37, wherein the pharmaceutically acceptable carrier is suitable for topical delivery.
  - 68. The method of claim 37, wherein the effective compound is in the form of a dosage unit, such that said dosage unit contains 10 to 1500 mg of the compound.

- 69. The method of claim 37, wherein the effective compound is in the form of a dosage unit that is a tablet or capsule.
- 70. The method of claim 37, wherein the host is a human.